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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/035,662	12/28/2001	John M. Stewart	4726-I-CON	4618
22442	7590	11/02/2004	EXAMINER	
SHERIDAN ROSS PC 1560 BROADWAY SUITE 1200 DENVER, CO 80202			KAM, CHIH MIN	
			ART UNIT	PAPER NUMBER
			1653	

DATE MAILED: 11/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/035,662

Applicant(s)

STEWART ET AL.

Examiner

Chih-Min Kam

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 August 2004.
2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 16-18 is/are pending in the application.
4a) Of the above claim(s) _____ is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 16-18 is/are rejected.
7) ☐ Claim(s) _____ is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
10) ☒ The drawing(s) filed on 06 May 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 12/28/01.
4) ☒ Interview Summary (PTO-413)
Paper No(s)/Mail Date. 20041027.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 16, 19 and 22, and the compound of Pya-Bip-Atmp in the response and amendment filed August 5, 2004 is acknowledged. In the amendment, claims 1-15 and 19-84 have been cancelled, and claim 16 has been amended. The product of Group I (claim 16) and the process of Group II (claims 17 and 18) are related as product and process of use, and a structure search for Pya-Bip-Atmp indicates the compound is free of prior art, thus, the process claims (claims 17-18) are rejoined with the product claim (claim 16). An Examiner's Amendment was proposed during a telephone interview with Robert Traver on October 27, 2004 (See Interview Summary), however, the proposed amendment was not accepted. Thus, an Office Action follows.

Informalities

The disclosure is objected to because of the following informalities:

2. The specification recites the term "37∞C" as the temperature for incubation, the symbol "∞C" (see page 16, lines 30; page 17, line 3) for the degree of centigrade is not correct.

Appropriate correction is required.

3. The specification recites Figs. 1-8 at page 19, line 1. However, there is no Fig. 8 submitted. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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4. Claims 17-18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inhibiting tumor growth of small cell lung cancer (SCLC) in an animal in need of such inhibition by administering the compound of Pya-Bip-Atmp, does not reasonably provide enablement for a method of inhibiting tumor growth in an animal in need of such inhibition, or inducing apoptosis of cancer cells by administering the compound of Pya-Bip-Atmp. The specification does not enable a person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 17-18 are directed to a method of inhibiting tumor growth in an animal in need of such inhibition, or inducing apoptosis of cancer cells by administering the compound of Pya-Bip-Atmp. The specification, however, only discloses cursory conclusions without data supporting the findings, which state that the present invention provides anti-cancer agents (ACA) comprised of a range of novel amino acid derivatives (e.g., Pya-Bip-Atmp) and small peptides having the ability to inhibit growth of SCLC (small cell lung cancer) and certain other tumor cell lines in standard *in vitro* tests, as well as certain monomeric peptides that show inhibition of tumor growth *in vivo*; a method inhibiting cancer by administering to a subject afflicted with cancer a therapeutically effective amount of one or more of the compounds; and the compounds function by stimulation of cell death in the tumor cells (page 1, line 30-page 2, line 14). There are no indicia that the present application enables the full scope of the claims in view of a method of treating tumor growth or inducing apoptosis of cancer cells by administering Pya-Bip-Atmp as discussed in the stated rejection. The present application does not provide sufficient teaching/guidance as to how the full scope of the claims is enabled. The factors considered in

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determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breadth of the claims, the presence or absence of working examples, the state of the prior art and relative skill of those in the art, the predictability or unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breadth of the claims:

The breadth of the claims is broad and encompasses a method of treating tumor growth of various cancers, or inducing apoptosis of cancer cells by administering Pya-Bip-Atmp.

However, the use of Pya-Bip-Atmp in the treatment of various cancers and inducing apoptosis of cancer cells are not adequately described or demonstrated in the specification.

(2). The absence or presence of working examples:

The specification describes synthesis of various anti-cancer agents (EXAMPLES I-XVIII); anti-tumor activity of Pya-Bip-Atmp against SCLC *in vitro* (Table 2, EXAMPLE XIX); an assay of measuring apoptosis in cultured cells (EXAMPLE XX); and inhibition of tumor growth *in vivo* in nude mice using certain anti-cancer agents (EXAMPLE XXI; Table 4; Figs. 1-7). However, the working examples do not demonstrate the claimed methods in association with various cancers or inducing apoptosis of cancer cells using Pya-Bip-Atmp.

(3). The state of the prior art and relative skill of those in the art:

The prior art (references cited at page 1 of the specification) teaches certain cancers such as SCLC have a neuroendocrine phenotype, and their growth is stimulated by neuropeptides; antagonists of several peptides (e.g., bradykinin, substance P) have been used in experimental

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treatment of models of SCLC in animals, and crosslinked dimers of certain bradykinin antagonists peptides are efficacious both *in vitro* and *in vivo* against SCLC and other tumors. However, the anti-tumor activity of Pya-Bip-Atmp is not related to bradykinin (see Table 2), and the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide teachings on the use of Pya-Bip-Atmp and its effect in the treatment of various cancers or inducing apoptosis of cancer cells.

(4). Predictability or unpredictability of the art:

The claims encompass a method of inhibiting tumor growth in an animal in need of such inhibition, or inducing apoptosis of cancer cells by administering the compound of Pya-Bip-Atmp. However, the treatment of various cancers and inducing apoptosis of cancer cells using Pya-Bip-Atmp are not adequately described in the specification, the invention is unpredictable regarding the effect of Pya-Bip-Atmp in the claimed method.

(5). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed to a method of inhibiting tumor growth in an animal in need of such inhibition, or inducing apoptosis of cancer cells by administering the compound of Pya-Bip-Atmp. The specification indicates anti-tumor activity of Pya-Bip-Atmp against SCLC *in vitro* (Table 2, EXAMPLE XIX); an assay of measuring apoptosis in cultured cells (EXAMPLE XX); and inhibition of tumor growth *in vivo* in nude mice using certain anti-cancer agents (EXAMPLE XXI; Table 4; Figs. 1-7). However, the specification has not demonstrated the compound has anti-tumor activity against various cancers, nor has indicated the compound induces apoptosis of cancer cells. Moreover, there are no working examples indicating the use

of the compound in treating various cancers *in vitro* or *in vivo*, or inducing apoptosis of cancer cells. Since the specification does not provide sufficient teachings on the use and effect of Pya-Bip-Atmp in the treatment of various cancers or inducing apoptosis of cancer cells, thus it is necessary to carry out further experimentation to assess the effect of the compound in the claimed method, the experimentation is undue because further research is required to determine an effective amount of the compound in the treatment of various cancers.

(6). Nature of the Invention

The scope of the claim encompasses inhibiting tumor growth, or inducing apoptosis of cancer cells by administering the compound of Pya-Bip-Atmp, but the specification does not provide sufficient teachings on the use of the compound in the treatment. Thus, the disclosure is not enabling for the reasons discussed above.

In summary, the scope of the claim is broad, the working example does not demonstrate the claimed method associated with various cancers, the teaching in the specification is limited, and the effect of compound in the treatment of various cancers and inducing apoptosis of cancer cells are unpredictable, therefore, it is necessary to carry out further experimentation in the use of the compound in claimed methods.

5. Claims 17 and 18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 17 and 18 are directed to a method of inhibiting tumor growth in an animal in need of such inhibition, or inducing apoptosis of cancer cells by administering the compound of Pya-Bip-Atmp. While the specification indicates that the invention provides anti-cancer agents (ACA) comprised of a range of novel amino acid derivatives (e.g., Pya-Bip-Atmp) and small peptides having the ability to inhibit growth of SCLC (small cell lung cancer) and certain other tumor cell lines in standard *in vitro* tests, as well as certain monomeric peptides that show inhibition of tumor growth *in vivo*; a method inhibiting cancer by administering to a subject afflicted with cancer a therapeutically effective amount of one or more of the compounds; and the compounds function by stimulation of cell death in the tumor cells (page 1, line 30-page 2, line 14), the specification does not disclose the use of Pya-Bip-Atmp (M296) in inhibiting tumor growth of various cancers or inducing apoptosis of cancer cells. The specification only demonstrates Pya-Bip-Atmp has anti-tumor activity against SCLC *in vitro* (Table 2, EXAMPLE XIX), it does not indicate the compound has anti-tumor activity against various cancers either *in vitro* or *in vivo*, nor demonstrates the compound induces apoptosis of cancer cells, although an assay of measuring apoptosis in cultured cells is described (EXAMPLE XX). The anti-tumor activity of Pya-Bip-Atmp against SCLC *in vitro* does not provide original descriptive support for a method of inhibiting tumor growth in an animal or inducing apoptosis of cancer cells. The disclosure of Pya-Bip-Atmp in the inhibition of tumor growth against SCLC *in vitro* do not meet the written description provision of 35 USC 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the ‘written description’ inquiry, whatever is now claimed.” (See

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page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.) The lack of representative examples and teachings for a method of inhibiting tumor growth in an animal in need of such inhibition, or inducing apoptosis of cancer cells by administering Pya-Bip-Atmp as encompassed by the claims, applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise terms that a skilled artisan would not recognize applicants were in possession of the claimed invention.

Therefore, only those embodiments described and disclosed meet the written description requirement and not the full breadth of the claim meets the written description provision of 35 USC 112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.) Applicants are directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 16-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claim 16 is indefinite because the claim recites a compound of Pya-Bip-Atmp without indicating its full name, thus it is not clear what the compound is. A fully spelled out word should be indicated for Pya-Bip-Atmp.

8. Claims 17-18 are indefinite because the claim lacks an essential step in the method of inhibiting tumor growth or inducing apoptosis of cancer cells. The missing step is an effective amount of the compound administered. Claim 18 is included in this rejection for being dependent on a rejected claim and not correcting the deficiency of the claim from which it depends.

Conclusion

9. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached at 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Chih-Min Kam, Ph. D.
Patent Examiner

A handwritten signature in dark ink, appearing to read 'Chih-Min', followed by a long, horizontal, wavy line that extends to the right.

CMK
October 27, 2004